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In re Application of	
Weiss et al.	
Application Number	Filed
08/359945	12.20.94

Paper No. #37

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(12) **United States Patent**
Weiss et al.

(10) **Patent No.: US 6,294,346 B1**
(45) **Date of Patent: Sep. 25, 2001**

(54) **USE OF MULTIPOTENT NEURAL STEM CELLS AND THEIR PROGENY FOR THE SCREENING OF DRUGS AND OTHER BIOLOGICAL AGENTS**

(75) Inventors: **Samuel Weiss**; **Brent Reynolds**, both of Calgary (CA); **Joseph P. Hammang**; **E. Edward Baetge**, both of Barrington, RI (US)

(73) Assignee: **Neurospheres Holdings, Ltd.**, Alberta (CA)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **08/484,406**

(22) Filed: **Jun. 7, 1995**

Related U.S. Application Data

(63) Continuation-in-part of application No. 08/385,404, filed on Feb. 7, 1995, now abandoned, and application No. 08/376,062, filed on Jan. 20, 1995, now abandoned, and application No. 08/359,945, filed on Dec. 20, 1994, now abandoned, and application No. 08/338,730, filed on Nov. 14, 1994, now abandoned, and application No. 08/311,099, filed on Sep. 23, 1994, now abandoned, and application No. 08/270,412, filed on Jul. 5, 1994, now abandoned, and application No. 08/149,508, filed on Nov. 9, 1993, now abandoned, which is a continuation-in-part of application No. 07/726,812, filed on Jul. 8, 1991, now abandoned, said application No. 08/961,404, is a continuation of application No. 07/961,813, filed on Oct. 16, 1992, now abandoned, which is a continuation-in-part of application No. 07/726,812, said application No. 08/376,062, is a continuation of application No. 08/010,829, filed on Jan. 29, 1993, now abandoned, which is a continuation-in-part of application No. 07/726,812, said application No. 08/359,945, is a continuation of application No. 08/221,655, filed on Apr. 1, 1994, now abandoned, which is a continuation of application No. 07/967,622, filed on Oct. 28, 1992, now abandoned, which is a continuation-in-part of application No. 07/726,812, said application No. 08/338,730, is a continuation-in-part of application No. 07/726,812, said application No. 08/311,099, is a continuation-in-part of application No. 07/726,812, said application No. 08/270,412, is a continuation-in-part of application No. 07/726,812.

(51) **Int. Cl.**[7] **G01N 33/554**; C12N 5/00

(52) **U.S. Cl.** **435/7.21**; 435/368; 435/377; 435/375

(58) **Field of Search** 435/7.21, 368, 435/378, 377, 375

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(57) **ABSTRACT**

A culture method for determining the effect of a biological agent on multipotent neural stem cell progeny is provided. In the presence of growth factors, multipotent neural stem cells are induced to proliferate in culture. The multipotent neural stem cells may be obtained from normal neural tissue or from a donor afflicted with a disease such as Alzheimer's Disease, Parkinson's Disease or Down's Syndrome. At various stages in the differentiation process of the multipotent neural stem cell progeny, the effects of a biological agent, such as a virus, protein, peptide, amino acid, lipid, carbohydrate, nucleic acid or a drug or pro-drug on cell activity are determined. Additionally, a method of screening the effects of biological agents on a clonal population of neural cells is provided. The technology provides an efficient method for the generation of large numbers of pre- and post-natal neural cells under controlled, defined conditions. The disclosed cultures provide an optimal source of normal and diseased neural cells at various developmental stages, which can be screened for potential side effects in addition to testing the action and efficacy of different biological agents.

12 Claims, 3 Drawing Sheets